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EXAMINER	
KEMMERER, ELIZABETH	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/541,953	JO, HANJOONG	
	Examiner	Art Unit	
	Elizabeth C. Kemmerer, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *7-12 and 17-28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,13-16 and 29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 July 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/18/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 10 March 2008 is acknowledged. The traversal is on the ground(s) that Weber et al. do not anticipate the claimed invention. Specifically, Applicant argues that Weber et al. teaches the use of native monomers of BMPs as BMP antagonists. Applicant further argues that Weber et al. fail to teach or suggest polypeptides derived from a CAN-like protein. Finally, Applicant criticizes Weber et al. for being directed to ossification processes instead of inflammation. This is not found persuasive because the first claimed invention does not require a CAN-derived protein. Furthermore, while claim 1 requires that the antagonist be present in an amount effective to inhibit or reduce vascular inflammation, the claim is directed to a product. The amount of antagonist disclosed by Weber et al. would inherently be in an amount effective to inhibit or reduce vascular inflammation since it has the activity of antagonizing BMP.

The requirement is still deemed proper and is therefore made FINAL.

Claims 7-12 and 17-28 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10 March 2008.

Applicant's election of the species of SEQ ID NO: 1 in the reply filed on 10 March 2008 is acknowledged. Because applicant did not distinctly and specifically point out

the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-6, 13-16, and 29 are under examination.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Specifically, the title does not refer to bone morphogenic protein antagonists or bone morphogenic protein receptor antagonists.

The disclosure is objected to because of the following informalities: The brief description of the drawings fails to refer to parts F-H of Figure 5.

Appropriate correction is required.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 29 refers to the polypeptide of SEQ ID NO: 1. However, SEQ ID NO: 1 is a nucleic acid sequence. Therefore, it is unclear what Applicant is claiming.

Page 3 of the specification indicates that SEQ ID NO: 1 corresponds to chordin. Therefore, for the purposes of examination, claim 29 will be interpreted as reading on a pharmaceutical composition comprising at least a portion of a chordin polypeptide. However, this treatment of claim 29 does not relieve Applicant from the requirement to address the discrepancy noted in this rejection.

35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 13-16, and 29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed invention wherein the active agent is a bone morphogenic protein-4 antagonist or a bone morphogenic protein-4 receptor antagonist, does not reasonably provide enablement for the claimed invention wherein the active agent inhibits other bone morphogenic proteins. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to compositions comprising an antagonist of any bone morphogenic protein or any bone morphogenic protein receptor, wherein the composition has the activity of inhibiting or reducing vascular inflammation. The specification clearly provides a nexus between antagonizing the binding of bone

morphogenic protein-4 to its receptor in vascular cells and inhibition of vascular inflammation. However, the specification does not establish that other bone morphogenic proteins are involved. The relevant literature reports examples of polypeptide families wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Tischer et al. (U.S. Patent 5,194,596) establishes that VEGF (a member of the PDGF, or platelet-derived growth factor, family) is mitogenic for vascular endothelial cells but not for vascular smooth muscle cells, which is opposite to the mitogenic activity of naturally occurring PDGF which is mitogenic for vascular smooth muscle cells but not for vascular endothelial cells (column 2, line 46 to column 3, line 2). The differences between PDGF and VEGF are also seen *in vivo*, wherein endothelial-pericyte associations in the eye are disrupted by intraocular administration of PDGF but accelerated by intraocular administration of VEGF (Benjamin et al., 1998, Development 125:1591-1598; see Abstract and pp. 1594-1596). Even more relevant is the finding of Vukicevic et al. (1996, PNAS USA 93:9021-9026) who disclose that OP-1, also known as BMP-7, has the ability to induce metanephrogenesis, whereas closely related BMP-2 and TGF-β1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). See also Massague, who reviews other members of the TGF- β family (1987, Cell 49:437-8, esp. p. 438, column 1, second full paragraph to the end).

Due to the large quantity of experimentation necessary to determine which other BMP antagonists have the required activity, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the

same, the complex nature of the invention, the contradictory state of the prior art, the unpredictability of which BMP has a specific activity unrelated to bone, and the breadth of the claims which fail to recite specific BMPs or antagonists, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 6, 13, 14, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/56879 (Weber et al.; published 28 September 2000). Weber et al. teach a pharmaceutical composition comprising a modified bone morphogenic protein-4, which is a bone morphogenic protein antagonist. See p. 10, lines 18-24, and the paragraph bridging pp. 12-13. While Weber et al. do not specifically teach that the antagonist is present in an amount sufficient to inhibit or reduce vascular inflammation, they do teach that the antagonist interferes with the binding of native bone morphogenic protein to its receptor (paragraph bridging pp. 12-13), and thus the composition of Weber et al. inherently has the required activity. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Similarly, although Weber et al. do not explicitly state that the

receptors are vascular cell bone morphogenic protein receptors, the receptors taught by Weber et al. are inherently vascular cell bone morphogenic protein receptors.

Regarding claim 13, Weber et al. teach the composition further comprising a pharmaceutically acceptable carrier at p. 16, lines 14-27. Regarding claim 14, Weber et al. teach microspheres at p. 16, line 21, which meets the limitation of a "medical device." Finally, claim 16 requires that the release of the antagonist occurs over time. Since the time is not specified, and reads on any length of time including very short periods of time, Weber et al. also anticipates claim 16.

Claims 1, 3-6, 13, and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by De Robertis et al. (US 5679783; issued 21 October 1997).

De Robertis et al. teach a pharmaceutical composition comprising chordin protein or a fragment thereof in combination with a pharmaceutically acceptable carrier. See col. 2, line 65; col. 3, lines 9-13; paragraph bridging col. 8-9. De Robertis et al. explicitly teach that chordin is a BMP-4 antagonist at the paragraph bridging col. 6-7. Although De Robertis et al. do not explicitly specifically teach that the antagonist is present in an amount sufficient to inhibit or reduce vascular inflammation, they do teach that the antagonist interferes with the binding of native bone morphogenic protein to its receptor (paragraph bridging col. 6-7), and thus the composition of De Robertis et al. inherently has the required activity. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)). Similarly, although De Robertis et al. do not explicitly state that the receptors are vascular cell

bone morphogenic protein receptors, the receptors taught by De Robertis et al. are inherently vascular cell bone morphogenic protein receptors.

Regarding claim 29, while De Robertis et al. do not teach SEQ ID NO : 1, it is reasonable to interpret claim 29 as being directed to a composition comprising chordin polypeptide, as discussed in the rejection under 35 U.S.C. § 112, second paragraph, above. Therefore, De Robertis et al. also anticipates claim 29.

35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/56879 (Weber et al.; published 28 September 2000) in view of Hunter et al. (US 5716981; issued 10 February 1998).

As discussed above, Weber et al. teach a pharmaceutical composition comprising a modified bone morphogenic protein-4, which is a bone morphogenic protein antagonist. See p. 10, lines 18-24, and the paragraph bridging pp. 12-13. Weber et al. further teach that the composition inhibits vascularization (pp. 15-16), and thus are anti-angiogenic agents which may be useful in treating tumors.

Weber et al. do not teach the compositions in combination with a vascular stent.

However, the prior art routinely coated vascular stents with anti-angiogenic factors which may be useful for treating tumors. See Hunter et al., col. 4, third and fourth paragraphs.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the composition of Weber et al. by adsorbing it onto a stent as disclosed by Hunter et al. with a reasonable expectation of successfully obtaining a new tumor treating device. Such was obvious because it constitutes a simple substitution of one known, equivalent element for another to obtain predictable results.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number

is (571) 272-0874. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D. can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ECK

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646